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Skin hypersensitivity following application of tissue adhesive (2-octyl cyanoacrylate)

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ABSTRACT

Tissue adhesives are commonly used for skin closure in both surgical and nonsurgical specialties. Although they are very well tolerated, tissue adhesives can induce a localized allergic response in 0.5% to 14% of patients. Allergic response can result in wound dehiscence, patient discomfort, increased healing time, and suboptimal esthetic results. We present two cases of allergic reaction to anterior neck incisions following topical application of tissue adhesives. The patients were managed with local wound care, steroid administration, and one with subsequent revision surgery. Clinicians who routinely use tissue adhesives should understand the incidence, risk factors, and management of allergic reaction to these products.

KEYWORDS Allergy; Dermabond; hypersensitivity reaction; skin closure; skin reaction; tissue adhesive

Skin adhesives are frequently used for wound closure. Advantages include added strength to wound closure, microbial barrier protection, and patient comfort, convenience, and cosmesis.[1–3] One common skin adhesive available for use is 2-octyl cyanoacrylate (Dermabond™). Dermabond is indicated for closely approximated surgical skin wounds and cleansed traumatic lacerations.[4] It is contraindicated in areas of infection and in mucosal surfaces/junctions of skin and mucosa, as well as in patients with a hypersensitivity to cyanoacrylate, formaldehyde, or benzalkonium.[4] Typically, skin adhesives are generally very well tolerated; however, there have been rare reports of adverse reactions. Infection, hypersensitivity reactions, wound dehiscence, pruritus, and skin blistering are potential adverse side effects of its use. Skin reactions can present immediately or in a delayed fashion.[5] This report describes two incidents of allergic hypersensitivity reaction to skin adhesive following topical application in head and neck surgery.

CASE DESCRIPTIONS

Two women presented for evaluation of primary hyperparathyroidism. Workup included serum parathyroid hormone, calcium levels, and a nuclear medicine parathyroid SPECT scan *(Table 1)*. Both underwent an uncomplicated transcervical approach to their parathyroid adenoma. Closure was undertaken in a standard layered fashion, followed by 4-0 Monocryl running subcuticular closure with topical application of Dermabond. The first patient experienced significant pain, pruritus, and swelling associated with the surgical incision *(Figure 1)*. She was treated with intravenous diphenhydramine and steroids, and an unsuccessful attempt was made to remove the skin adhesive, despite following the manufacturer's recommendations. In the second case, the patient denied pruritus or pain associated with the reaction. Postoperatively, skin sloughing, necrosis, and superficial infection were observed, requiring a course of antibiotics. Local wound care was prescribed until resolution. She refused any additional revision surgery *(Figure 2)*.

DISCUSSION

We present two cases of severe localized allergic reaction to Dermabond. Dermabond is a strong adhesive utilized as a topical wound dressing or skin closure technique alone or in combination with other techniques.[6] Dermabond was initially approved by the Food and Drug Administration for wound closure in 1998 and has been utilized by both surgical and nonsurgical specialties.[7] The initial product studies

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demonstrated a low infection rate and minimal side effects. For the last 20 years, Dermabond has been used with great clinical success.

One uncommon risk of topical skin adhesives is allergic reaction.[8] Recent studies suggest that allergic reaction is due to 2-octyl cyanoacrylate while in the liquid form.[9] An allergic response to cyanoacrylate materials has been reported to be as high as 17.5% in the general population.[10] Development of an allergic skin reaction typically occurs after a patient is sensitized. Spencer et al noted that sensitization to cyanoacrylates occurs by way of industry, acrylic nail applications, and increasingly surgical/medical uses.[11] Asai showed that allergic contact dermatitis to 2-octyl cyanoacrylate was highly attributable to previous sensitivity reactions.[12]

Table 1. Patient variables for two cases of hypersensitivity to tissue adhesive

	Case 1	Case 2
Age (years)	40	79
Preoperative PTH (pg/mL)	109	283
Serum calcium (mg/dL)	10.4	11.4
Parathyroid adenoma	Left inferior excised	Right inferior excised
Transcervical approach	+	+
Application of skin adhesive	Dermabond	Dermabond
Interval to symptoms (hours)	9	6
Length of stay (days)	2	1
Revision surgery	+	−

PTH indicates parathyroid hormone.

An increased dosage of tissue adhesive as well as application to abraded skin appears to increase the severity of the reaction.[13] It is reported that allergic reactions to topical skin adhesives are low because the polymerization of cyanoacrylates removes the allergen from solution, reducing the response. Water works as the nucleophile that drives the polymerization reaction, which occurs within minutes of application. When there is reduced moisture, the polymerization of the surgical glue is slowed and the sensitization to the allergen is potentially increased. Humidity and moisture may play a key role in allergic responses.[14]

Case reports have emerged detailing adverse local and systemic reactions after tissue adhesive usage. Ricci et al documented a case of diffuse cutaneous allergic reaction to Dermabond that required emergency evaluation and treatment.[15] Ghaffar et al presented two cases of contact dermatitis that mimicked a knee implant reaction after orthopedic surgery.[16] The reactions presented with pruritus and rash several weeks after surgery. Subsequent patch testing showed significant reactivity to the Dermabond solution. Nigro et al recently evaluated a cohort of patients who underwent breast surgery with cyanoacrylate products.[17] Twelve patients developed significant dermatitis reactions. Two patients had previous known allergies to cyanoacrylate. The incidence of allergic response to tissue glues was 14% in their study. Those who experienced reactions were confirmed with scratch testing. The authors cautioned against the use of cyanoacrylate due to the high incidence of adverse skin reactions. In another study, Nakagawa utilized Dermabond Advanced as a final occlusive dressing following breast surgery.[18] The incidence of contact dermatitis was calculated to be 7% of study participants. The authors concluded that application of Dermabond Advanced should be avoided in patients who have a history cyanoacrylate sensitivity.

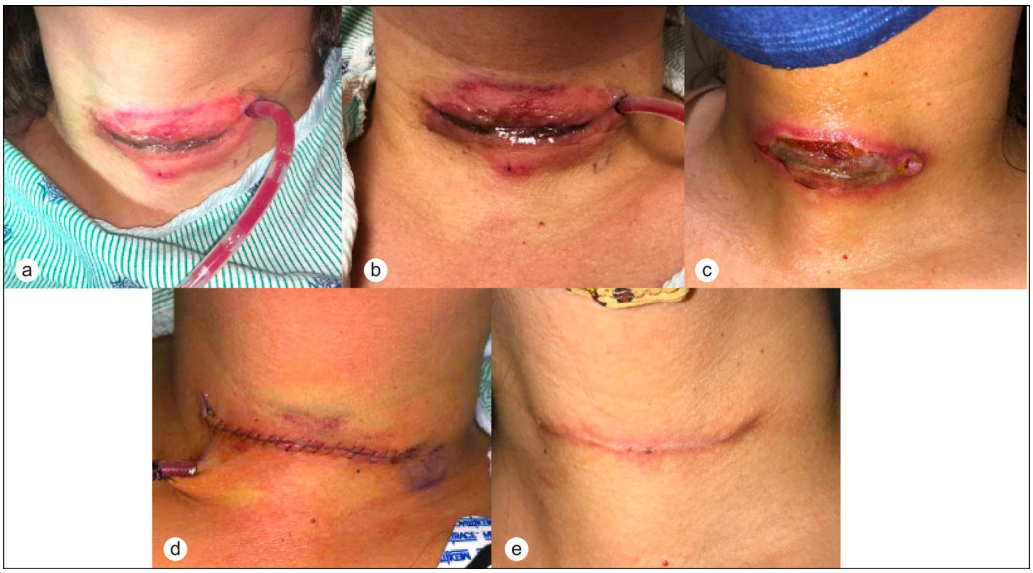

Figure 1. Skin reaction for Case 1 at **(a)** 9 hours after application, **(b)** 36 hours after application, and **(c)** 1 week after application. Scar revision both **(d)** postoperatively and **(e)** 1 month later.

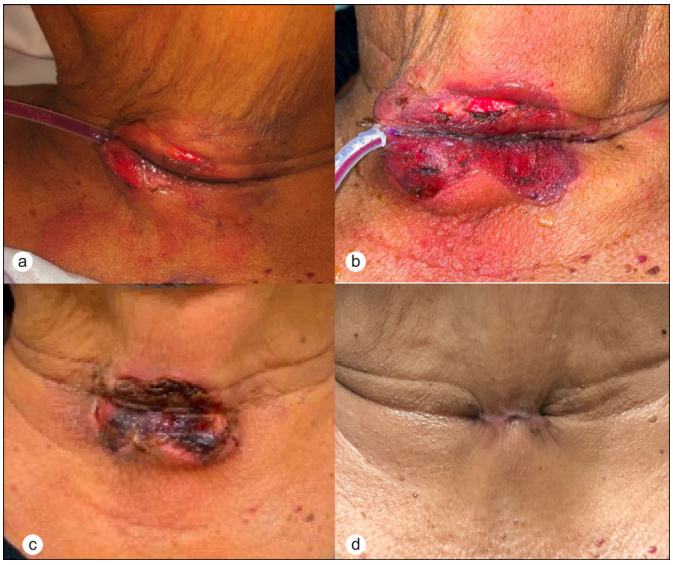

Figure 2. Skin reaction for Case 2 at **(a)** 6 hours after application, **(b)** 24 hours after application, **(c)** 1 week after application, and **(d)** 3 months postoperatively.

The management of tissue adhesive allergy begins by recognizing allergic response vs infection.[8] Systemic steroids should be utilized when indicated. If feasible, the offending product should be quickly removed to help aid in resolution. However, this tends to be difficult with the potential to cause wound dehiscence.[8]

In summary, allergic reactions to tissue adhesives lead to increased healing time, patient discomfort, and suboptimal esthetic results. Clinicians should be aware of the pathophysiology, incidence, risk factors, and management of these reactions. We recommend patient screening for prior reactions to cyanoacrylate products. Dermal allergy testing should be performed on high-risk populations exposed to these products regularly. Prompt removal of the offending products can aid in hastening recovery in combination with oral or intravenous steroids. Finally, surgical revision can improve cosmetic outcomes once the reaction has subsided.

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